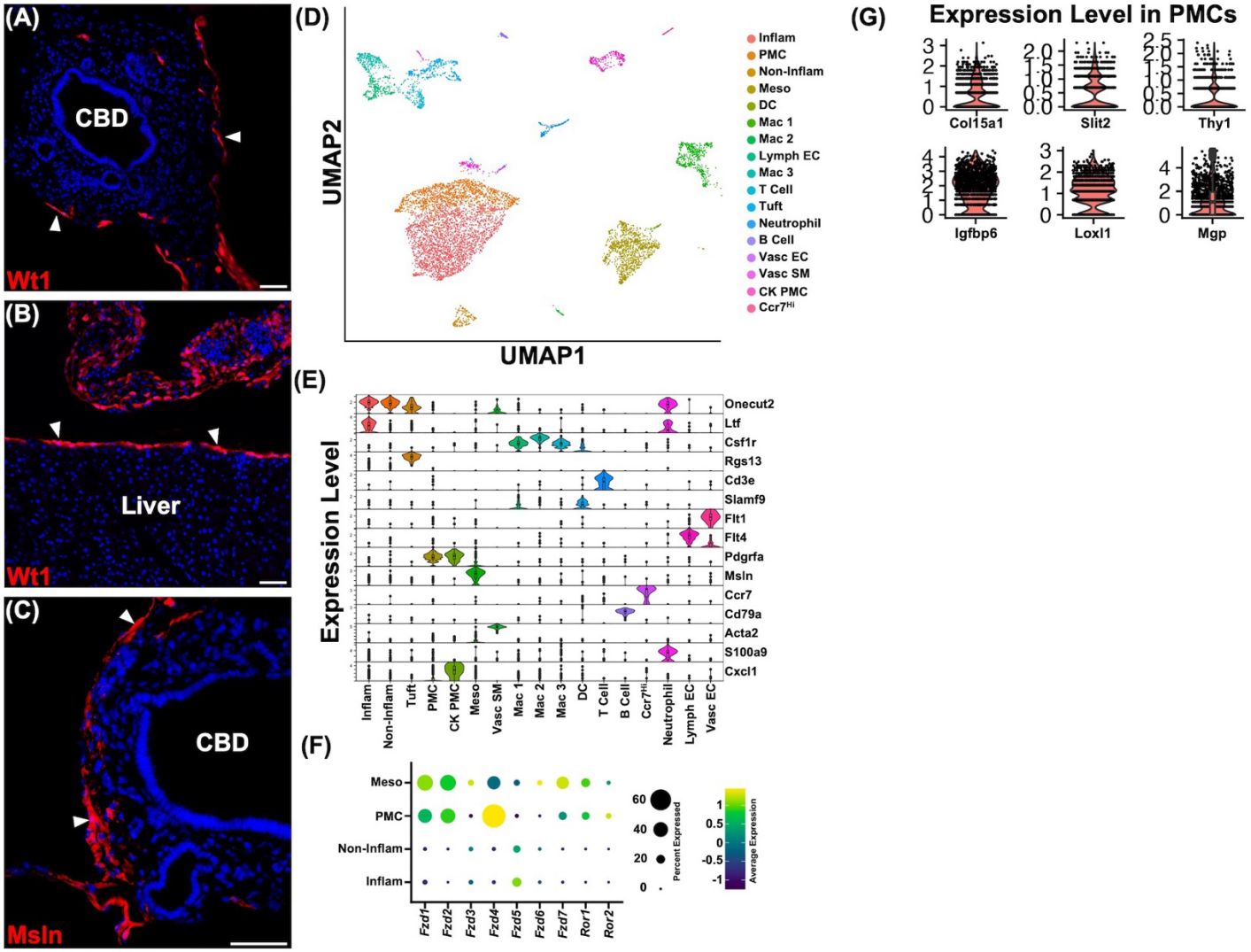
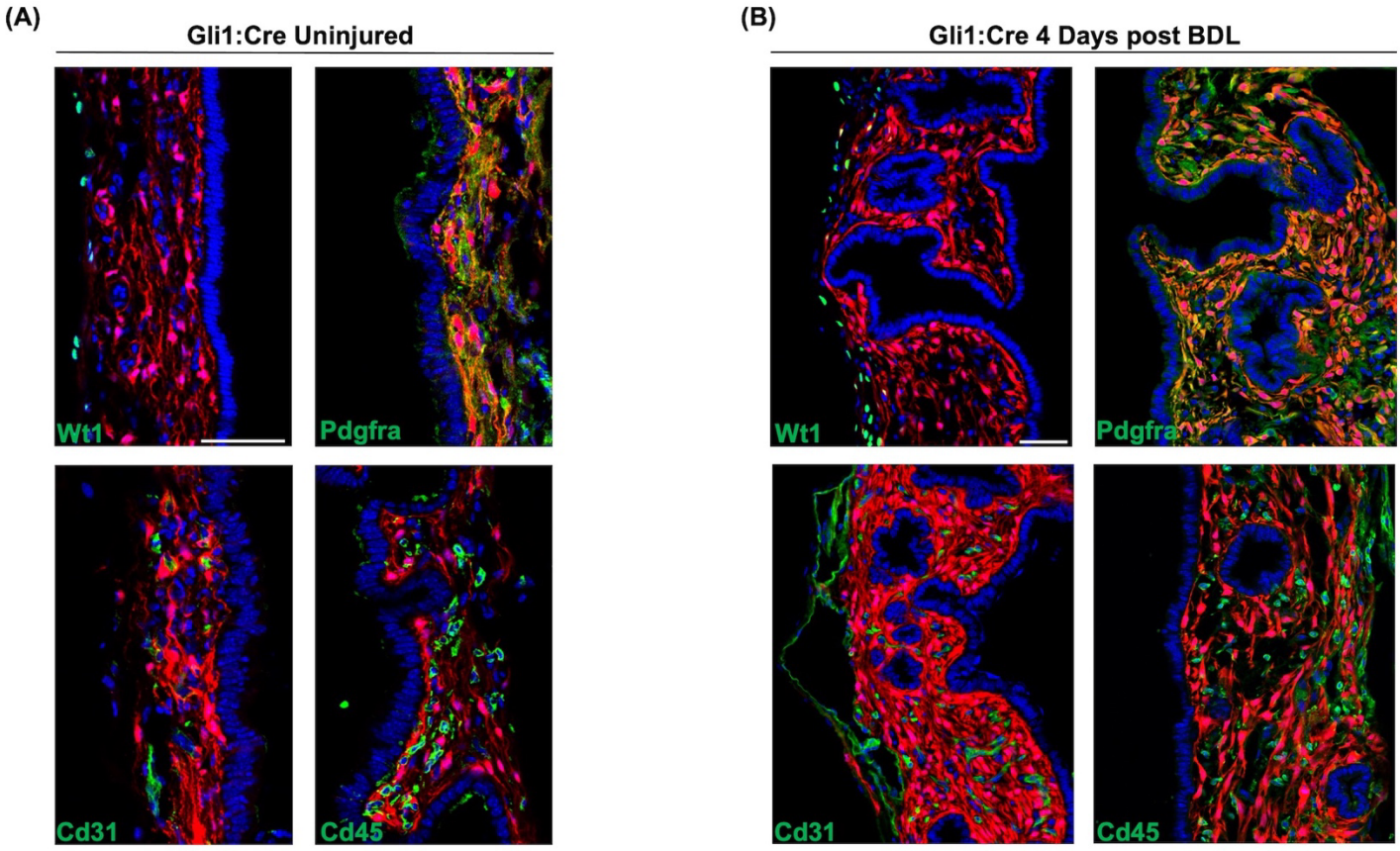
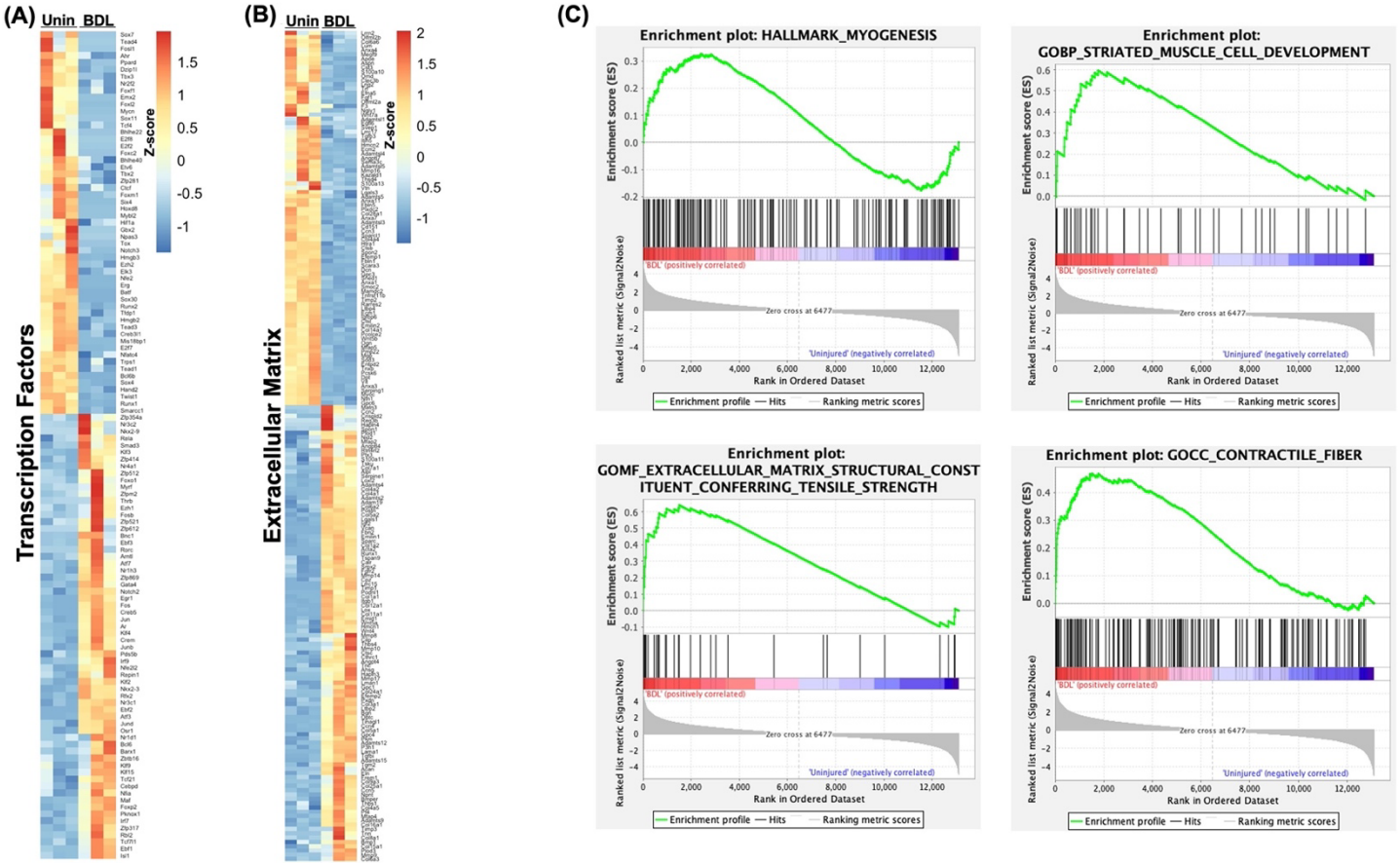


Supplemental Figure 1. Mesothelial markers and single-cell sequencing analysis.

(**A** and **B**) *Wt1:Cre*^{ERT2}; *Rosa26:lox-STOP-lox-tdTomato* animals after tamoxifen mediated recombination showing mesothelial cells around the CBD (**A**, arrowheads) or on the liver surface (**B**, arrowheads) (n = 3). (**C**) *Msln* antibody staining of the CBD showing staining around the CBD (arrowheads) (n = 3). (**D**) UMAP showing different cell types found in the murine CBD. (**E**) Violin plot showing marker gene expression for each cluster. (**F**) Dot plot showing expression of different *Fzd* receptors in cholangiocyte and mesenchymal populations. (**G**) Violin plots showing expression level of indicated genes in PMCs that are elevated in intrahepatic portal mesenchyme. Scale bars, 50 μm.

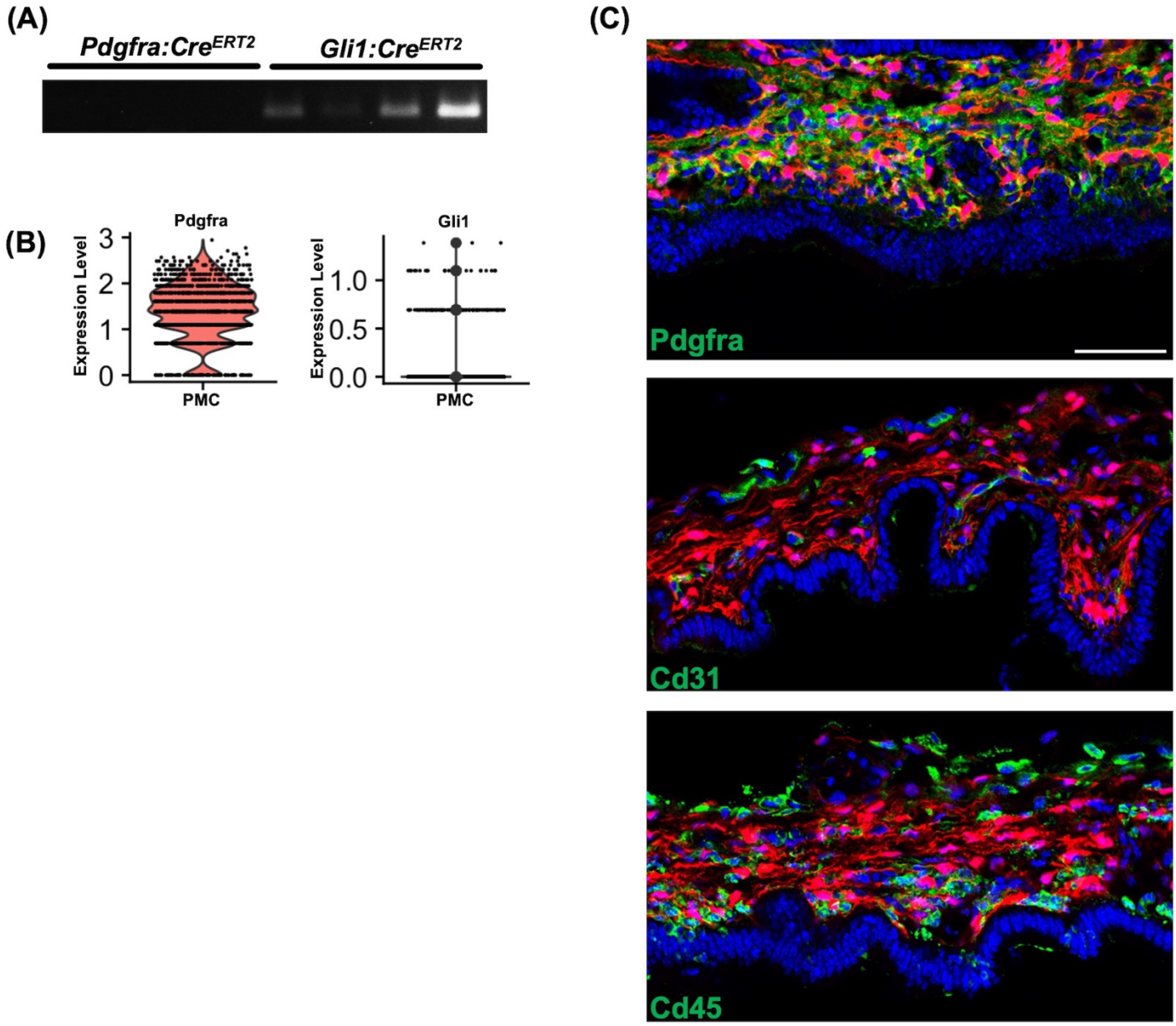


Supplemental Figure 2. Specificity of Gli1:Cre^{ERT2} in uninjured and 4 day BDL animals.
(**A** and **B**) *Gli1:Cre^{ERT2}*; *Rosa26:lox-STOP-lox-tdTomato* 14 days after tamoxifen (**A**) or 4 days post BDL (**B**) were stained with the indicated antibodies to show that recombination is specific to PMCs. Scale bars, 50 μm.



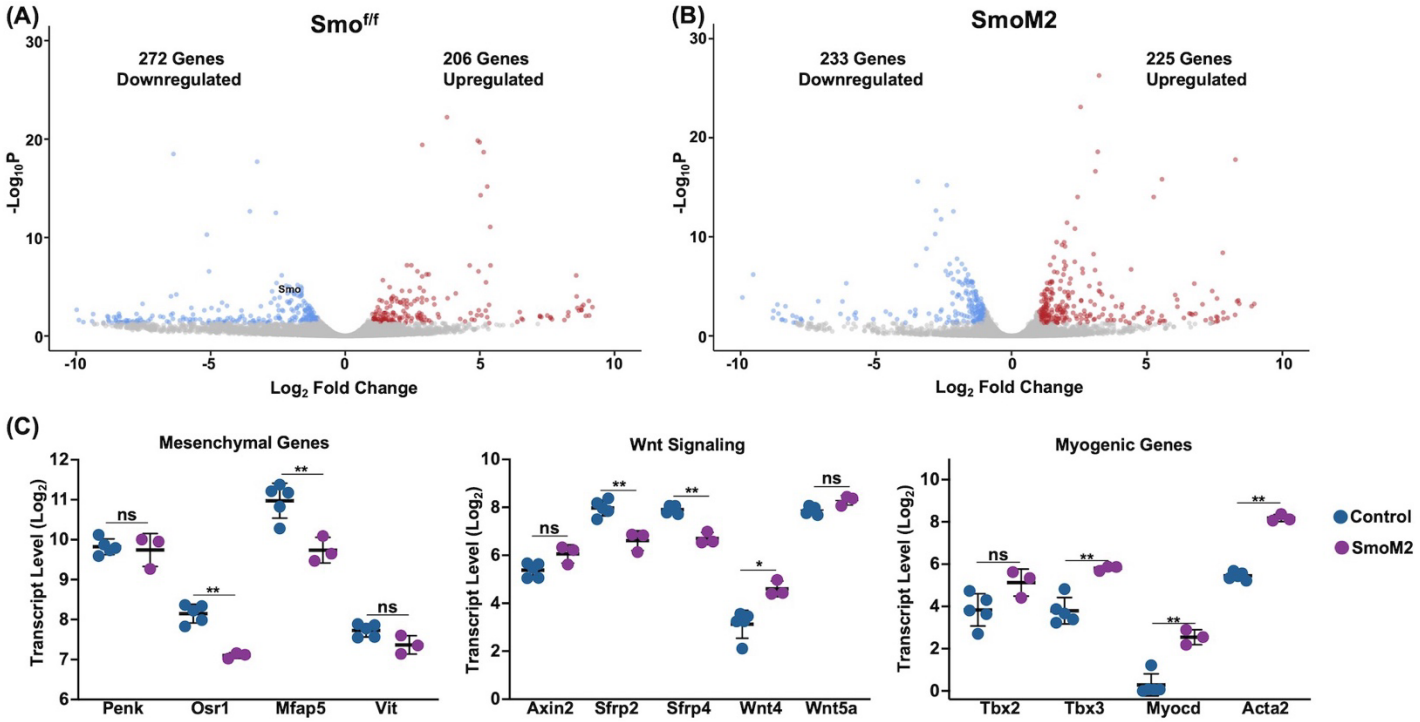
Supplemental Figure 3. Transcriptomic analysis of injured peribiliary mesenchymal cells.

(**A**) Heatmap showing differentially expressed transcription factors between uninjured and 4 day BDL PMCs. (**B**) Heatmap showing differentially expressed extracellular matrix genes between uninjured and 4 day BDL PMCs. (**C**) Gene set enrichment analysis of indicated gene sets.



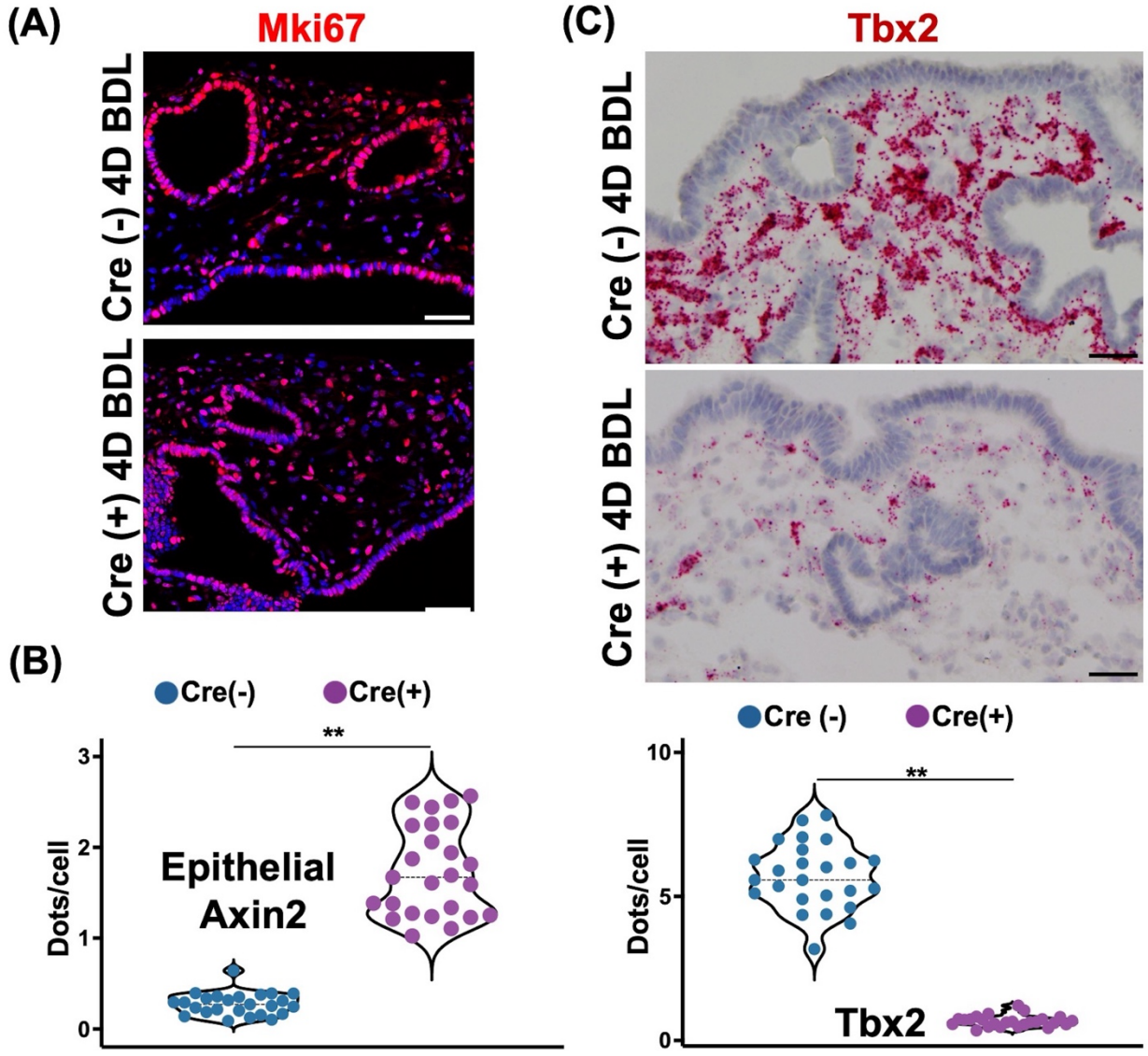
Supplemental Figure 4. Specificity of Pdgfra:Cre^{ERT2}.

(**A**) PCR for *Smo$^{f/f}$* allele from sorted PMCs from *Pdgfra:Cre^{ERT2}*; *Rosa26:lox-STOP-lox-tdTomato; Smo$^{f/f}$* and *Gli1:Cre^{ERT2}*; *Rosa26:lox-STOP-lox-tdTomato; Smo$^{f/f}$* showing inefficient recombination in *Gli1:Cre^{ERT2}* animals. (**B**) Violin plot showing the expression level of *Pdgfra* vs *Gli1* in PMCs from single-cell sequencing. (**C**) Staining with indicated antibodies to show that recombination is specific to PMCs.



Supplemental Figure 5. Analysis of PMC *Smo* gain and loss function

(**A**) Volcano plot showing the differential expression of PMC loss of *Smo* compared to control. (**B**) Volcano plot showing the differential expression of PMC gain of *Smo* compared to control. (**C**) Plots showing expression of mesenchymal, Wnt, and myogenic genes in *Smo* gain of function compared to control. ns = not significant *p <0.05, **p<0.005 by Benjamini-Hochberg (FDR).



Supplemental Figure 6. Analysis of *β-catenin* loss of function.

(**A**) *Mki67* staining of *Pdgfra:Cre^{ERT2}; β-catenin$^{f/f}$* and *β-catenin$^{f/f}$* animals 4 days post BDL. (**B**) Quantification of epithelial *Axin2 in situ* signal in *Pdgfra:Cre^{ERT2}; β-catenin$^{f/f}$* and *β-catenin$^{f/f}$* animals 4 days post BDL (n = 5). (**A**) *Tbx2 in situ* from *Pdgfra:Cre^{ERT2}; β-catenin$^{f/f}$* and *β-catenin$^{f/f}$* animals 4 days post BDL and quantification (n = 5 for each group). **p<0.005 by Student's t-test.